Case Report Rapport de cas

Pneumomediastinum and subcutaneous emphysema in a cat associated with necrotizing bronchopneumonia caused by feline herpesvirus-1

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Abstract — This report describes a 1-year-old cat with acute dyspnea. Thoracic radiography revealed a pneumomediastinum and severe subcutaneous emphysema. Lower airway surgical exploration was unable to determine the cause. At postmortem examination, acute necrotizing bronchopneumonia and fibrinonecrotic tracheitis due to feline herpesvirus-1 were diagnosed.

Résumé — Pneumomédiastin et emphysème sous-cutané chez un chat associés à une bronchopneumonie nécrosante causée par le virus de la rhinotrachéite féline. Ce rapport décrit un chat âgé de 1 an atteint de dyspnée aiguë. Une radiographie thoracique a révélé un pneumomédiastin et un emphysème sous-cutané aigu. Une exploration chirurgicale des voies respiratoires inférieures n'a pas pu déterminer la cause. À l'autopsie, une bronchopneumonie nécrosante aiguë et une trachéite fibrinonécrosante causées par le virus de la rhinotrachéite féline ont été diagnostiquées.

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Pneumomediastinum is a rare condition in which free air or gas is present in the mediastinum. Because the mediastinum communicates with the subcutaneous tissues in the neck through the thoracic inlet and with the retroperitoneum through the aortic hiatus, gas will spread between those 3 regions and cause subcutaneous emphysema and/or pneumoretroperitoneum (1). Air accumulating within the mediastinum may also progress into the pericardial sac (2). Pneumothorax can develop when mediastinal air ruptures through the mediastinal tissues (2). Pneumomediastinum may result from sharp penetrating trauma to the neck, or from mediastinal infection with gas-forming bacteria, but it is usually secondary to accidental or iatrogenic trauma to the lower airways, the marginal alveoli, or the esophagus (2,3). After alveolar rupture air may spread by a retrograde route through the lung interstitium and thus cause pneumomediastinum without pneumothorax. In humans several infectious agents have been identified as causes of pneumomediastinum (4–7). In cats, however, little is known about infectious agents causing pneumomediastinum. In this report we describe a unique case of pneumomediastinum associated with necrotizing bronchopneumonia due to feline herpesvirus-1 (FHV-1).

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Case description

A 1-year-old neutered male Siamese cat was presented at our institution because of severe progressive dyspnea and coughing of 4 days duration. On the second day the referring veterinarian performed radiography and respiratory endoscopy; the findings were unremarkable. Initial treatment (nasal rinsing, antitussive aerosol, steroid therapy) did not improve the clinical symptoms. The cat had been vaccinated against FHV-1 5 mo ago. On referral, the cat was dehydrated and had severe inspiratory dyspnea, tachycardia, subcutaneous emphysema of the neck and the thoracic and abdominal regions. Whole blood hematology and biochemistry revealed moderate dehydration [packed cell volume (PCV) 43%, total protein (TP) 99 g/L] and mild azotemia [blood urea nitrogen (BUN) 18.15 mmol/L, creatinine 160 mmol/L].

Right-left lateral (Figure 1a) and ventro-dorsal (Figure 1b) radiographic projections of the thorax revealed large amounts of gas in the subcutaneous tissues surrounding the thorax and abdomen and, in the fascial planes of the neck. The cranial mediastinum showed an irregular pattern of mixed opacity (primarily soft tissue and gas). The entire esophagus was dilated with gas. The pulmonary vasculature appeared decreased in size. A radiographic diagnosis of severe subcutaneous emphysema, pneumomediastinum, megaesophagus, and suspicion of hypovolemia was made. The megaesophagus was considered secondary to respiratory distress and the hypovolemia due to dehydration.

Conservative medical treatment consisted of cage rest, oxygen supplementation (nasal tube), and intravenous fluid therapy. Rapid further clinical deterioration changed the treatment plan and an emergency surgical exploration of the lower airways was performed. During neck exploration and cranial sternotomy the cervical and thoracic trachea, bronchi, lungs, and esophagus

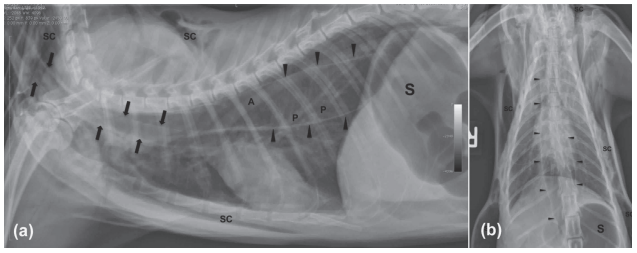

Figure 1. (a) Right-left lateral radiograph of the thorax. Gas is visible in the subcutaneous tissue around the thorax and dissecting the fascial planes of the neck (SC). The esophagus is filled with gas over its entire length (arrowheads). The walls of the trachea are visible (arrows). The stomach (S) is moderately distended by gas. (b) Ventro-dorsal radiograph of the thorax. A large amount of gas is present in the subcutaneous tissues surrounding the thorax and in the fascial planes of the neck (SC). The wall of a dilated esophagus is visible (arrowheads).

were carefully inspected and submersed. No leakage of air could be detected. The cranial mediastinum was opened and a thoracic drain was placed. Postoperative intravenous fluids, antibiotics, analgesics, and oxygen supplementation were continued. Only small amounts of air and fluid were evacuated from the thorax during the following 8 h. Inspiratory and expiratory dyspnea was present and a gradual decline in oxygenation below 90% was measured by pulse oximetry. The patient was intubated and kept on ventilator support. After initial stabilization the oxygenation again declined. At this time arterial blood gas values were severely disturbed [pH 7.15, reference interval (RI): 7.35 to 7.45], (PaO_2 = 52 mmHg, reference value > 80 mmHg), ($PaCO_2$ = 59 mmHg, RI: 35 to 45 mmHg) and the owner elected euthanasia.

At necropsy, extensive subcutaneous and intermuscular emphysema was found in the neck region, the abdominal wall, and the proximal parts of the limbs. The lungs were moderately and diffusely hemorrhagic and edematous. The esophagus was distended with gas. A bacteriological culture of the lung was negative. Tissue samples from lung and trachea were fixed in formalin and embedded in paraffin. Histopathology of the lung revealed a multifocal to coalescing necrotizing bronchopneumonia (Figure 2a). Amphophilic intranuclear inclusions were found in sequestered bronchial and bronchiolar epithelial cells. The tracheal mucosa was covered with fibrinonecrotic material. Sections of lungs and trachea were immunolabelled for FHV-1 antigen with a monoclonal mouse antibody against FHV-1 and a commercial kit (Dakocytomation envision system-HRP; Abd Serotec, Oxford, UK). In the lung, FHV-1 positive labelling was found mainly in sequestered bronchial and bronchiolar epithelial cells and in alveolar macrophages and pneumocytes in necrotic alveolar septa (Figure 2b). Also many tracheal epithelial cells labelled positive for FHV-1.

Discussion

Feline herpesvirus-1 is an alphaherpesvirus of cats causing mainly upper respiratory tract and ocular disease worldwide (8). Latency following the acute phase of the disease occurs in approximately 80% of infected animals (9), resulting in episodes of reactivation associated with virus shedding and in some cases, clinical disease. FHV-1 typically produces necrotizing lesions

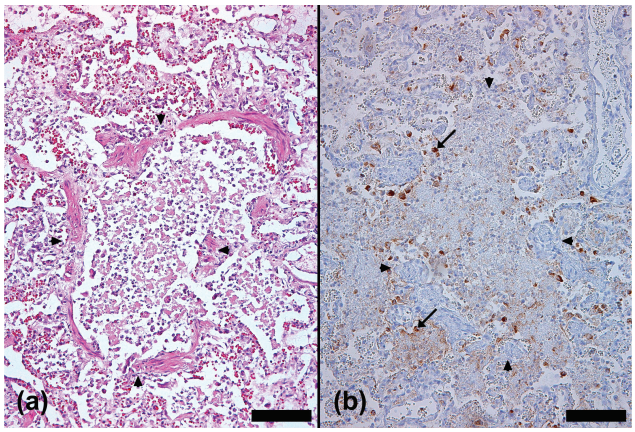

Figure 2. Cat lung. (a) Necrotic bronchiolus (arrowheads) filled with degenerate neutrophils, fibrin, and necrotic material. Hematoxylin & eosin stain. Original magnification, 200×. (b) FHV-1 antigen expressed within sequestered bronchial epithelial cells and alveolar macrophages (arrows). Centrally in this figure, a bronchiolus is present (lined by arrowheads), which is surrounded by alveolar spaces. Immunohistochemistry, anti-FHV-1 antibody, Envision + system-HRP kit mouse; chromogen: DAB; counterstain: Mayer's hematoxylin. Original magnification, 200×.

originating from cytolysis due to active virus replication. As a consequence of this cytolytic effect, lesions such as corneal and gastrointestinal perforation develop (10). Occasionally, primary viral pneumonia may occur, mainly in young or immunodeficient animals (11,12). To our knowledge, pneumomediastinum has not been reported as a complication of FHV-1 infection.

In human medical literature, many cases of pneumomediastinum are reported listing a variety of causes including esophagal, tracheal, bronchial or alveolar trauma, inflammation or neoplasia (13–15), but also, in rare cases, spontaneous pneumomediastinum independent of any underlying cause (16). Reported infectious causes of pneumomediastinum in humans are staphylococcal and *Mycoplasma pneumoniae* pneumonia (4–6) and in 1 case *Pneumocystis carinii* pneumonia (7). In cattle, pneumomediastinum is described as a rare complication of pulmonary emphysema (17). In dogs and horses, it is mostly mentioned as a consequence of trauma (18,19). Pneumomediastinum in cats is reported in association with tracheal tear or rupture mainly due to intubation (20) and overinflation during anesthesia (21–23). In this case, tracheal tear or rupture was considered an important possibility since this cat previously had undergone an anesthetic procedure. For respiratory endoscopy the patient is most often not intubated, but the referring veterinarian had also performed a gastroscopy which does necessitate tracheal intubation. Diagnosis of tracheal tear or rupture is commonly made by computed tomography, bronchoscopy, or surgical exploration. Radiography had been performed and computed tomography was not possible in an emergency situation. Respiratory endoscopy had already been performed and found inconclusive. Endoscopy is not always reliable to identify the site and extent of tracheal disruption (24).

Due to the patient's unstable condition, respiratory endoscopy and computed tomography of the area were not performed. Instead, emergency surgical exploration was pursued to rapidly identify and treat a tracheal lesion. During induction and intubation an inspection of the pharyngeal area was performed. After

midline exploration of the cervical trachea a cranial sternotomy was performed to evaluate the thoracic part. No macroscopically visible tracheal lesions were found that could explain the subcutaneous emphysema and pneumomediastinum. The cervical and thoracic trachea (along with lungs and esophagus) were carefully immersed in physiologic saline solution and evaluated for leakage. No air leakage could be found and, at necropsy there was no site of tear or rupture; these findings ruled out any tracheal tear severe enough to cause such extensive subcutaneous emphysema.

On histopathology, necrotic tracheal epithelial cells were covered by a layer of fibrin and necrotic debris, intermixed with degenerative neutrophils that migrated trough the mucosa (exocytosis). Several tracheal epithelial cells labeled positive for FHV-1 on immunohistochemistry. In the tracheal submucosa there was a diffuse moderate infiltrate of lymphocytes, plasma cells and macrophages, but this layer, as well as other tracheal structures was intact. Semi-serial histopathological sections of the trachea showed the same pattern. These arguments make the possibility of a tracheal rupture or perforation unlikely. In the history of the cat the owners did not mention any possible trauma. Hair was clipped around the cervical and thoracic regions, and no penetrating lesions were identified on the skin. Previously, blood was sampled from the cephalic vein by the referring veterinarian. But, apart from a small localized skin discoloration, no lesion was present that could explain the amount of subcutaneous emphysema. In order to accumulate the amount of air in the mediastinum and subcutis, as observed in this case, through vein puncture, detectable trauma to the skin and vein should have occurred.

Careful inspection at necropsy did not reveal any perforating trauma. Pharyngeal and cranial esophageal perforation can also cause extensive subcutaneous emphysema. But when food content or saliva migrates into the surrounding tissue, a rapidly progressing inflammation will be obvious. During intubation the pharyngeal area was inspected and during surgical exploration the esophagus was also examined. There was no inflammation surrounding these organs.

Air can travel along sheaths of pulmonic blood vessels into the mediastinum after it has entered the interstitial tissue of the lung by alveolar rupture (1). Also, in lungs with bronchiolar necrosis, inhaled air will come into the interstitial tissue. In the case presented here, the presence of necrosis of bronchioli and alveoli, together with the exclusion of other causes of the pneumomediastinum, suggests the same mechanism of migration of air as described by Macklin (1). On radiographic examination, extensive subcutaneous emphysema was present. Generally, causes of primary subcutaneous emphysema are trauma with rupture of the larynx, trachea or oesophagus, surgery, and infection. Based on the history (no previous surgery or known trauma) and the surgical exploration (negative for leaks with intact mediastinum), these possibilities can be excluded. Subcutaneous emphysema caused by *Clostridium* spp. was ruled out due to the absence of other lesions such as cellulitis or myonecrosis. We therefore conclude that the subcutaneous emphysema was secondary to the bronchopneumonia.

Pneumomediastinum can be readily diagnosed on radiography by identification of the mediastinal great vessels and esophageal and tracheal walls that are normally not seen but become visible because of the negative contrast provided by surrounding gas. In the present study, free mediastinal gas enhanced visualization of the adventitial surface of the trachea but not the main vascular structures (aortic arch, cranial vena cava, brachiocephalic trunk, and left subclavian artery) because of the presence of subcutaneous gas creating a heterogeneous aspect of the cranial mediastinum.

The effect of a small amount of free gas in the mediastinum alone is usually minimal (25). In most patients the underlying cause of the pneumomediastinum influences the animal more than the pneumomediastinum itself. Commonly the most serious possible sequel of massive pneumomediastinum is pneumothorax (2). This complication was anticipated and a thoracic drain was placed. Since the evacuation of the thoracic drain was only minimal, it is possible that the pneumomediastinum persisted despite the surgical attempt to bring the mediastinum into contact with the pleural cavity. In that regard, persisting respiratory problems might be attributable to the "airblock" phenomenon. Under experimental conditions, it has been shown that the accumulation of large amounts of gas in the mediastinum can cause increased mediastinal pressure, resulting in decreased venous return to the heart (26). Another explanation for the failure to stabilize this patient's respiratory problems can be found when mediastinal air enters the pericardial cavity, resulting in pneumopericardium. Radiographs of the thorax and postmortem investigation, however, ruled out this condition. A decisive matter is that mediastinal air spreading to the interstitium of the lungs, decreases pulmonary compliance. While artificial ventilation would be necessary to achieve expansion of the alveoli, ventilation would also increase the amount of air entering the mediastinum and start a potentially lethal vicious circle. However, considering the severe pulmonary lesions at the postmortem examination, the clinical deterioration of the cat was likely due to insufficient lung function.

Repeated blood sampling by needle puncture or the placement of a durable arterial catheter for blood gas evaluation of the oxygenation was not considered due to practical reasons and the poor condition of the patient. Evaluation of the respiratory condition by means of pulsoximetry was, however, a reliable alternative in this case (27).

In conclusion, in cats, as in human medicine, pneumonia should be considered as a possible underlying cause of pneumomediastinum. The authors hypothesize that FHV-1 infection of the lungs was the primary cause in this case. CVJ

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